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Circular Letters:

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<u>Tuberculosis, a Hazard for Personnel of the Staffs of General Hospitals and</u> <u>Measures for Control in the Navy</u>: Personnel of the staffs of general hospitals experience the real hazard of becoming infected by the causative organisms of tuberculosis as a result of their employment. The National Tuberculosis Association and other agencies have repeatedly reported the existence of this hazard. Progressive schools of medicine and nursing, and many hospitals, in efforts directed toward its elimination, have adopted simple measures such as, (1) routine tuberculin tests and chest roentgenograms for staff personnel, (2) routine roentgenographic examinations of the chest of each patient admitted, and (3) rigidly enforced precautions against communicable disease in the care of tuberculous patients. Certain foreign hospitals, in addition, are employing inoculations of the bacillus of Calmette and Guerin (BCG vaccine).

* A survey was made of several Navai Hospitals for the period from 1 March 1945 to 1 June 1946, and although the staffs of those hospitals containing tuberculosis centers experienced a somewhat higher morbidity rate for pulmonary tuberculosis than the others, not a single hospital surveyed was found not to show any cases of tuberculosis among its staff.

In addition to constant vigilance in the exercise of precautions against communicable disease, there remain two directions toward which Naval hospitals may direct their attention in controlling this hazard when the necessary equipment and personnel are available, namely, (1) the routine examination of staff personnel, and (2) the routine examination of all patients and outpatients.

1. <u>Examination of Staff Personnel</u>: The following schedule is offered as a guide for use when it is found possible to initiate the program for the routine examination of all personnel on the staff and of all new staff members immediately upon reporting to the hospital.

(a) A tuberculin test. The standard two-test method, or, if preferred, a single test using 0.0001 mg. P.P.D. may be used. In either instance the tests <u>must be intradermal</u> as described in "Diagnostic Standards 1940," National Tuberculosis Association.

(b) A roentgenographic examination of the chest, preferably by the 35 mm. technic with re-examination by the 14x17 inch technic, if indicated by suspicious findings.

(c) Positive reactors to tuberculin should receive a roentgenographic examination of the chest once a year.

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(d) Negative reactors to tuberculin should be retested at intervals of six months.

(e) Procedure to follow when a positive test is found in a person who upon the previous testing was negative:

(1) Complete physical examination, complete blood count, sedimentation rate, and sputum analysis if sputum is present.

(2) Removal from duty with tuberculous patients and reassignment elsewhere in the hospital.

(3) X-ray of the chest every three months for eighteen months.

(4) Close supervision for the purpose of observing early evidence of tuberculous disease.

(f) Entries should be made in the Health Record of each individual examined, giving the studies carried out and the results observed.

2. Examination of Patients and Outpatients: Routine roentgenographic examinations of the chest of persons admitted to Navy hospitals and treated in outpatient departments are an integral part of tuberculosis case-finding. The finding of cases of tuberculosis helps to protect the health of staff personnel through the prompt isolation of such patients. In such a project all patients receive the examination as soon as practicable. It is believed that hospitals will find this type of case-finding study particularly rewarding.

The roentgenographic examination should be made by the 35 mm. technic with re-examination by the 14x17 inch technic if indicated by suspicious findings.

In this connection it is noted that although an annual roentgenographic examination of the chest of Navy and Marine Corps personnel under the age of 30 has been required since June, 1944, and, of <u>all</u> personnel since September 1946, there are many in the Service who have never received the examination; and Fleet Reserve, retired personnel, and many veterans will be found not to have received such an examination for years. Examination of outpatients should reveal cases of tuberculosis among the dependents of Service personnel and, by their discovery, contribute to the health of the Navy. (Preventive Med. Div., Bumed)

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Relationship of Cellular Content of Bronchial Secretions and Tuberculosis: In the course of a study of bronchial secretions for cancerous cells the authors were at first baffled by the presence in some cases of small or large clusters of unusual epithelial cells. Except for the fact that they always contained cilia, they often bore a superficial resemblance to cells found in a low-grade bronchogenic epidermoid carcinoma. When the final conclusions were being formulated in these cases, it became apparent that those bronchial secretions exhibiting many such collections were from patients with pulmonary tuberculosis, and that secretions from patients with other diseases, and particularly chronic tracheobronchitis, bronchiectasis, and pulmonary abscess, usually presented a complete absence or at the most only one or two clusters of somewhat similar cells. This observation has proved to be of considerable practical significance, for by its use on several occasions it has been possible to make a presumptive diagnosis of pulmonary tuberculosis before learning the results from cultures for Mycobacterium tuberculosis. Furthermore, those patients in whom the tuberculous lesion was atypical and confused with primary bronchogenic carcinoma, have been spared an exploratory thoracotomy.

In a series of 210 examinations of bronchial secretions there were 57 cases of proved bronchogenic carcinoma, 47 of which revealed cancer cells in the bronchoscopically aspirated material. In the same series there were 13 cases considered clinically as carcinoma in which a cytological diagnosis of tuberculosis was made and in which the causative bacilli were later isolated. There was only one case in which a positive diagnosis of tuberculosis was made and in which a positive diagnosis of tuberculosis was made and in which a positive diagnosis of tuberculosis was made and in which the presence of this disease has not yet been substantiated.

The procedure used in obtaining the secretions and preparing the smears is exactly the same as that employed in the cytological study of secretions for bronchogenic carcinoma. At an ordinary bronchoscopy, secretions are secured in a regular or special collector (attached directly to the aspirator) from the bronchus or bronchi draining the suspected area. If the amount of material secured is scanty, all is smeared; but if it is abundant, it is first poured into a flat transparent dish and those portions streaked with blood or containing small grey particles are transferred to clean glass slides. Smears are made by the crush method using another slide, and the material is spread to a thickness of an ordinary blood smear. While still wet the slides are dropped into equal parts of 95 per cent alcohol and ether where they are left to fix for thirty minutes, after which they are stained by the Papanicolaou technic. Every portion of every slide is systematically examined first with 80 X and then with 400 X magnification, using subdued light.

Ordinarily, in cases of pulmonary tuberculosis, there is little difficulty in arriving at a correct diagnosis, but sometimes the lesion is so situated and the accompanying signs and symptoms are so atypical that its true nature is

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completely masked. This was well demonstrated in a case studied by the authors. The central position of the lesion and the lack of constitutional disturbances made the diagnosis of bronchogenic carcinoma a very good possibility. Tuberculosis, on the other hand, was not suspected until smears of bronchial secretions were examined cytologically, following which proper staining of the remaining secretions revealed acid-fast bacilli. Another case was very similar, except that repeated examinations of sputum failed to disclose tubercle bacilli and smears of two bronchoscopically removed secretions likewise failed to reveal the organisms. Because of this the suspicion that the lesion was cancerous and not tuberculous was entertained more and more until the cytological examination of bronchial secretions disclosed the structures that had been found to be associated with tuberculosis; and, later-the cultures of secretions for <u>M</u>, <u>tuberculosis</u> were found to be positive. It is in this type of case that cytological study of bronchoscopically removed secretions is of the greatest value for, if the lesion is cancerous, a pneumonectomy should be performed without delay but, if it is tuberculous, a thoracotomy is ordinarily contraindicated. The cytological examination is also of value when the patient has anthracosilicosis and in addition either apical tuberculosis or cancer which cannot be demonstrated by bronchoscopic examination.

It must be emphasized, however, that only a presumptive and not a definitive diagnosis of pulmonary tuberculosis can be made from a cytological study of bronchoscopically removed secretions, and that the isolation of M. tuberculosis is the only unequivocal criterion. But this same statement also holds for a diagnosis of tuberculosis based upon the histological study of tissue sections and yet that method is practiced routinely. In smears of bronchial secretions there are two elements which arouse a suspicion of pulmonary tuberculosis, namely, (1) the presence of numerous collections (three dozen or more in one slide) of ciliated epithelial cells and (2) the presence of giant cells of the Langhans' type. It is apparent that in patients with pulmonary tuberculosis whose bronchial secretions exhibit these cells there must be an ulceration of the epithelium of the bronchi before the tenth branching - the level of transition between ciliated and nonciliated epithelium. In the process of ulceration the cells break off in large numbers in clumps or singly, and, seemingly because they are spontaneously sloughed, their borders are always rounded. This is extremely important, for occasionally in cases other than tuberculosis, and as a result of trauma with the bronchoscope, single, or groups of, ciliated epithelial cells are seen, but the outer margins of these are always ragged and rough. The authors believe that the large cells with multiple nuclei are definitely Langhans' giant cells. (Am. Rev. Tuberc., Dec. '46 - P. A. Herbut and L. H. Clerf)

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<u>The Antibiotic Subtilin</u>: Subtilin is an antibiotic produced by some strains of <u>Bacillus subtilis</u>. It is a substance of low molecular weight which dialyzes through collodion membranes, and has the structure of a peptid. It is insoluble in 95 per cent alcohol but is readily soluble in 70 per cent alcohol. Subtilin dissolved in water gives a solution having a light yellow color and a pH of 4.55. It is precipitated at low salt concentrations and is soluble to an appreciable extent only in acid solutions. The antibiotic is probably a basic substance giving water-soluble salts. Subtilin is stable in dried form. Samples stored at room temperatures in the dark have retained their activity for months. Light has a destructive action on the antibiotic, particularly when it is in solution.

In vitro this antibiotic is effective chiefly against Gram-positive bacteria. A few Gram-negative organisms are equally as susceptible, as for example, <u>Neisseria gonorrhoeae</u> and <u>Neisseria catarrhalis</u>. However, the great majority of Gram-negative organisms are not susceptible unless concentrations considerably higher than usual are used. Acid-fast organisms, including <u>Mycobacterium tuberculosis</u>, are also susceptible to the antibiotic. The diseaseproducing organisms include <u>Bacillus anthracis</u>, <u>Corynebacterium diphtheriae</u>, <u>Diplococcus pneumoniae</u>, staphylococcus, streptococcus, <u>Neisseria gonorrhoeae</u>, and <u>Mycobacterium tuberculosis</u>.

Subtilin showed an extremely low toxicity for fragments of embryonic chick heart tissue cultivated <u>in vitro</u>. Under the conditions of the test the antibiotic was approximately 20 times more toxic to <u>Staphylococcus aureus</u> than to cells of chick heart tissue. This is equivalent to a toxicity index of 0.05, a remarkably low tissue toxicity for a germicidal agent.

A unit of subtilin is defined as that amount present in 1 c.c. of the highest dilution capable of killing <u>Staphylococcus aureus</u> in 10 minutes at 37° C. by the FDA (Food and Drug Administration) phenol coefficient method.

Subtilin was found to modify greatly the outcome of experimental infections in animals.

Mice inoculated with <u>Diplococcus pneumoniae</u> Type III and then treated with subtilin 9 hours later were quickly cured of the infection. All of the control animals died in from 24 to 36 hours after being given an injection of Type III pneumococcus. On the other hand, all of the treated mice survived after being given subtilin for only 48 hours.

Subtilin produced a powerful action on experimental anthrax infections in guinea pigs. Animals treated with the antibiotic 9 hours after being injected with anthrax bacilli were protected from the disease.

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It also proved to be very effective against <u>Streptococcus pyogenes</u> infections in mice. All of the control animals died within 11 hours whereas all of the treated animals survived and were apparently normal 2 weeks after treatment was discontinued.

Recovery was spectacular in mice given subtilin 9 hours after being infected, which was 5 hours before their expected death. At the time treatment was started recovery seemed impossible. The infection had been accompanied by diarrhea, ruffled fur, and prostration. After receiving 2 injections of subtilin, the diarrheal condition disappeared and the animals appeared to be almost normal. After the fourth injection, the animals looked and acted like healthy mice and devoured food freely.

The antibiotic proved effective also against <u>Staphylococcus</u> <u>aureus</u> infections in mice, but more was required than in the preceding experiment.

To date subtilin has produced a definite suppressive effect on experimental tuberculous infections in guinea pigs. Control animals examined 10 days after inoculation with the organism showed the presence of very large, indurated nodules at the site of inoculation. The nodules gradually softened, ulcerated, and discharged quantities of pus. On the other hand, treated animals showed either no nodules or, at most, only very slight swellings at the site of inoculation.

Both control and treated animals were sacrificed three weeks after being inoculated with the organism and examined internally. The control animals showed the presence of small necrotic areas in the liver and spleen. The spleens were at least twice normal size and in most cases even larger. The livers of treated animals did not show the presence of small necrotic areas and appeared normal in every respect. The spleens were either normal in size and appearance or only slightly enlarged and moderately granular.

Studies in animals on the treatment of tuberculosis with subtilin alone and in combination with certain sulfa drugs or other compounds are still in progress and more detailed information will be released at a later date.

The results leave no doubt that subtilin is a powerful antibiotic for the treatment of a number of infectious diseases caused by Gram-positive bacteria. The agent is relatively nontoxic to fragments of chick heart tissue cultivated <u>in vitro</u>, and toxic symptoms have not been observed in any of the treated animals, including those given doses as high as 100 mg. at one time. (From a paper presented at a recent meeting of the Antibiotics Study Section, National Institute of Health, USPHS, by A. J. Salle of the Department of Bacteriology of the University of California at Los Angeles)

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<u>The Antibiotic Tomatin</u>: Tomatin, an antibiotic agent that is present in the cultivated tomato plant, <u>Lycopersicon esculentum</u>, is capable of inhibiting the soil-borne fungus, <u>Fusarium oxysporum f. lycopersici</u>, that causes tomato wilt, an economically serious disease of this important food crop. Moreover, it has been found that the antibiotic effectiveness of tomatin is not limited to this one organism; it inhibits to an even greater extent cultures of certain human pathogenic fungi and bacteria.

The results of these preliminary investigations point to two interesting possibilities: (1) that tomatin may be responsible, either wholly or in part, for the resistance offered by certain tomato varieties to Fusarium wilt; and (2) that because of its marked inhibitory action upon several important human pathogens (particularly the fungi), tomatin may be of therapeutic value in the treatment of human infections that are caused by these organisms.

The academic and practical significance of the possibilities that have been mentioned have encouraged concerted efforts to isolate tomatin, to determine its structure, its origin, action, and fate in the tomato plant, and its toxicity to animals and humans, and to extend the investigation of its antibiotic spectrum to the largest practicable number of different pathogenic organisms. The major part of this program remains to be accomplished. The results reported here are based upon observations made with partially purified, but still impure preparations of tomatin.

Tomatin is present in highest concentration in tomato leaves, to a lesser extent in the roots, and to the least extent in the stems and fruit. In the laboratory preparation of tomatin it is preferable to use the leaves of the Red Currant tomato plant, <u>Lycopersicon pimpinellifolium</u>, a Peruvian variety that bears currant-sized fruit, since this variety is the richest source of tomatin so far discovered. For practical purposes, however, whole plants of any commercial variety may be used as the source of tomatin.

Crude tomatin preparations contain approximately 0.2 units of tomatin activity per mg. In numerous attempts to increase the potency of such preparations, fractions have been isolated which have potencies of from 1 to 2 units per mg. Unfortunately, because the procedures so far utilized have resulted in such prohibitive losses in total activity, they have been temporarily abandoned as impractical.

In aqueous solution (pH 5.5) in sealed ampoules, crude tomatin is able to withstand a temperature of 120° C. for at least 5 hours without detectable loss of antibiotic activity. Tomatin is dialyzable. Based on the study of crude preparations, tomatin is soluble in water at pH values below neutrality, is

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very soluble in absolute methanol, and exhibits progressively decreasing solubility in ethanol, isopropanol, and butanol.

Preliminary toxicity tests upon guinea pigs with a saline solution of a tomatin preparation containing 1.2 units per mg. have indicated that animals can tolerate the parenteral administration of as much as 10 mg. of such a preparation without fatal consequences, although unfavorable reactions are produced. The intravenous, intraperitoneal, or subcutaneous injection of a solution containing 1 mg. of crude tomatin induced no notable reaction. However, the intravenous injection of 10 mg. into each of two animals produced immediate symptoms of distress and swelling of the injected legs. The animals recovered from the systemic reaction within 24 hours, but the injected legs remained swollen. Both animals continued to gain weight, and one recovered completely within 4 days; the second animal suffered necrosis of the injected leg.

Tomatin has been found to be highly effective in vitro in inhibiting the human dermatophytic fungi, including species of <u>Trichophyton</u>, <u>Epidermophyton</u>, <u>Microsporum</u> and <u>Achorion</u>, and several of the fungi and yeast-like forms that cause internal disease, including species of <u>Monilia</u>, <u>Cryptococcus</u>, <u>Debaryomyces</u>, <u>Blastomyces</u>, <u>Coccidioides</u>, and <u>Histoplasma</u>. It is slightly. effective against both Gram-positive and Gram-negative bacteria, species of the fungi, <u>Fusarium</u>, <u>Penicillium</u>, <u>Aspergillus</u>, <u>Sporotrichum</u>, and <u>Monosporium</u>, and the <u>Actinomyces</u> pathogenic for plants. It is without effect upon the <u>Actinomyces</u> pathogenic for humans and the fungi responsible for the chromoblustomycoses. Tomatin-like substances have been found to be present also in certain plants other than the tomato. (From a paper presented at the recent meeting of the Antibiotics Study Section, National Institute of Health, USPHS, by T. D. Fontaine et al. of the Bureau of Agricultural and Industrial Chemistry and Bureau of Plant Industry, Soils, and Agricultural Engineering, Agricultural Research Center, Beltsville, Maryland)

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The Effect of Caronamide upon Penicillin Therapy of Experimental Pneumococcus and Typhoid Infections: It is now agreed that one of the major disadvantages of penicillin as a therapeutic agent is the rapidity with which the human and animal kidney excretes the drug from the plasma into the urine. Because of this rapid excretion, which occurs both by way of the renal tubules and the glomeruli, relatively large doses must be given every few hours if a detectable plasma concentration is to be maintained. To obtain higher concentrations of penicillin in the plasma, very much greater quantities are required. The administration of both diodrast and para-aminohippuric acid

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(PAH) simultaneously with penicillin has been used to decrease the excretion of penicillin. Both of these substances, however, must be given in large amounts by continuous intravenous infusion.

This report is on experiments demonstrating the effect of a chemical compound that has been reported by Beyer (Bumed News Letter of 14 February 1947) to offer a new approach to the problem of decreasing the urinary excretion of penicillin. The compound, 4'-carboxyphenylmethanesulfonanilide, has been called caronamide and will be referred to by this name. Unlike diodrast and PAH, which compete with penicillin on a mass-action basis for the penicillin transport mechanism of the renal tubular epithelium, caronamide does not appear to be excreted by the tubules and is, therefore, believed to suppress penicillin excretion by blocking the specific enzyme system responsible for penicillin transport through the tubular cells. Because tubular elimination is apparently not a factor in the excretion of caronamide it remains in the blood for a longer period of time than does either diodrast or PAH. Therefore, it is possible to use intermittent administration of caronamide to suppress the excretion of penicillin. For this purpose, the oral route of administration is effective since caronamide is rapidly absorbed from the gastro-intestinal tract.

The pharmacological experiments of Beyer et al., using dogs, demonstrated that the intravenous or oral administration of caronamide could suppress and even eliminate, the tubular excretion of penicillin when this antibiotic agent was given by either the intravenous or oral route. Although it was clearly indicated by these experiments that greater therapeutic activity could be expected, the actual increase in the in vivo bacteriostatic effect produced by the enhanced and prolonged plasma penicillin concentrations obviously could not be determined by that type of experiment. It was, therefore, considered desirable to design experiments in which animals would be infected with lethal doses of micro-organisms and treated with graded amounts of penicillin both alone and with caronamide. The survival rates in the groups of animals receiving various doses of penicillin with and without the drug were believed to offer a means of calculating the bacteriostatic dosageequivalents of penicillin alone and penicillin with the drug. The ratio of these penicillin dosage-equivalents then could be used as an estimate of the in vivo bacteriostatic advantage derived from the suppression of penicillin excretion by the administration of caronamide. With this in view tests were carried out using white Swiss mice weighing from 16 to 22 Gm. Strains of Type I pneumococcus and Eberthella typhosa were selected as test organisms for these experiments both because they produced satisfactory experimental infections in mice and because they were organisms having widely different sensitivities to penicillin.

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The experiments clearly demonstrated that <u>in vivo</u> bacteriostatic action may be achieved with much smaller doses of penicillin when this treatment is combined with the oral administration of caronamide. In addition, it has been shown that the administration of caronamide causes penicillin to attain higher levels in mouse plasma and to remain there for a longer time than when a similar amount of penicillin is administered alone. Since the drug has no demonstrable bacteriostatic action of its own and does not cause any enhancement of the <u>in vitro</u> bacteriostatic action of penicillin, it cannot be considered to act synergistically with this antibiotic agent. It is believed, therefore, that the increased effectiveness of intramuscularly administered penicillin results from the influence of caronamide on the duration and magnitude of penicillin plasma and tissue concentrations.

It is interesting to note that experiments with the two organisms used resulted in different equivalent-dosage ratios. These were 4 compared to from 6 to 16 for the experiments with E, typhosa and D, pneumoniae respectively. The plasma penicillin concentration curves, when considered with the relative penicillin sensitivities of the two cultures, offer an explanation for this observation. The intensity of penicillin therapy can be tentatively represented as a function of the area under a curve where the concentration of penicillin is plotted against time and the baseline is the minimal penicillin concentration having any bacteriostatic effect upon the test organism. In the case of the E. typhosa strain, this baseline was approximately 2 units and with the pneumococcus it was 0.0008 units. It can be seen that as the baseline is moved downward the area under the penicillin-caronamide curve increases disproportionally to that of the curve produced by the administration of penicillin alone. Thus it will be seen that the advantage produced by caronamide in penicillin therapy, though very considerable against organisms of relatively high resistance, becomes even greater against highly susceptible organisms.

Many bacterial infections that have been considered to be resistant to the usual clinical penicillin dosages have been found to be caused by bacteria sensitive to amounts of penicillin that, in these experiments, inhibited <u>E.</u> <u>typhosa</u>. Evans has reported that, of 66 strains of <u>E</u>, <u>typhosa</u>, all but one were inhibited completely by from 10 to 25 units of penicillin per ml. of culture medium. Although it is not possible to translate penicillin dosage in mice into dosage in man, it seems reasonable to expect therapeutic effects in man at plasma penicillin concentrations similar to those found to be effective in mice. The studies carried out by Crosson, Boger, Shaw and Miller have indicated that such plasma penicillin concentrations may be attained in man with moderate intramuscular doses of penicillin when caronamide is administered orally. It would, therefore, seem that the use of caronamide together with penicillin may offer a means of increasing the effectiveness of

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penicillin treatment and bringing more bacterial infections within the limits of practical penicillin therapy. (From a paper presented at a recent meeting of the Antibiotics Study Section, National Institute of Health, USPHS, by W. F. Verwey and A. K. Miller of the Department of Bacteriology of the Research Division of Sharpe and Dohme, Inc.)

<u>Penicillin Blood Levels Obtained in Dogs with Oil-Wax Preparations</u> of <u>Calcium Penicillin and Crystalline Sodium and Potassium Penicillin G</u>: Since the crystalline sodium and potassium salts of penicillin have become available, there has been widespread interest in their relative absorption and excretion rates in the body. Particular interest has centered in the comparative value of these and of the less pure calcium salt in penicillinoil-wax preparations for the prolongation of therapeutically effective blood levels.

Three plant-production lots of oil-wax preparations of crystalline sodium and three of crystalline potassium penicillin G have been compared with similar amorphous calcium penicillin preparations for their relative value in maintaining plasma penicillin levels in dogs. The plasma concentrations of penicillin have been determined in dogs at various periods up to 48 hours following the intramuscular administration of these preparations in single doses of 300,000 and 600,000 units. The calcium penicillin in oil and wax was the standard Romansky Formula at 300,000 units per c.c.; sodium G and potassium G preparations were made with crystalline salts, suspended in the same concentration of beeswax in peanut oil at potencies of both 300,000 and 600,000 units per c.c. All lots met FDA (Food and Drug Administration) specifications for potency.

The oil-wax preparations of crystalline sodium penicillin G used in this study appeared to be superior to those made with crystalline potassium penicillin G for the maintenance of 12- and 24-hour plasma levels.

Half the dose volume, through the use of twice the usual concentration of penicillin in oil and beeswax, that is, 0.5 c.c. of a preparation containing 600,000 units per c.c., appears entirely feasible and practical with the use of the crystalline salts of penicillin. The plasma levels obtained with this dosage were comparable to or better than those obtained with 1.0 c.c. of 300,000 units per c.c. of calcium penicillin in oil and wax, although not quite as well sustained as those obtained with 1.0 c.c. of the 300,000 units per c.c. concentration of the respective crystalline salts. (From a paper presented at a recent meeting of the Antibiotics Study Group, USPHS, by J.C. Burke of the Biological & Chemical Laboratories of E.R. Squibb & Sons)

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<u>A New Technic for Pulmonary Segmental Resection</u>: Doctors are confronted with few problems that are more serious than those presented by a patient suffering from bronchiectasis. The disease process, if untreated, is irreversible, progressive, and for most patients eventually causes death. On the other hand, of all chronic pulmonary diseases, the outcome in the case of bronchiectasis is one of the most hopeful for the reason that pulmonary resection affords not only alleviation of symptoms, but also cure in a high percentage of cases.

Although the fundamental pathology of primary bronchiectasis has been known for decades, only in recent years has the characteristic, distribution of the disease in bronchopulmonary segments been realized. The increasing use of bronchography and the detailed study of surgical specimens have shown that bronchiectasis is primarily a segmental disease and rarely involves an entire lobe. In addition, bronchiectasis tends to involve the bronchopulmonary segments in certain patterns. Basal segments of the lower lobes are most commonly involved. The lingula division of the left upper lobe and the bronchiof the right middle lobe are frequently found to be diseased along with the basal segments. The superior segment of the lower lobe, however, is rarely affected. Another very important pathological and clinical observation has been that the -distribution of primary bronchiectasis, as far as the affected segments are concerned, has usually reached its full extent at the time of diagnosis. Any progression of pulmonary involvement from this point on will not be through involvement of other segments by the bronchiectatic process, but by associated suppurative changes in the pulmonary parenchyma itself.

In recent years, many excellent anatomical studies along with increased surgical experience in resecting pulmonary tissue, have demonstrated that the bronchopulmonary segment is a surgical unit and lends itself to removal without undue technical difficulties or risk. As a result, segmental resection by a technic developed by the authors during the past year is now being used with increased frequency in the surgical treatment of bronchiectasis. Segmental resection not only eradicates all of the diseased segments, but it also eliminates the necessity of a sacrifice of uninvolved segments. This approach to the problem permits the accomplishment of two fundamental principles of surgery: (1) the cure of the patient; (2) the preservation of as much functional tissue as possible.

The purpose of this paper is to describe an original and new technic of segmental resection as employed in 23 operations in cases of bronchiectasis.

In bronchiectasis unisegmental disease is found less frequently than unilateral multiple segmental disease, and unisegmental disease is also less common than bilateral involvement. Of the last one hundred consecutive cases of

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primary bronchiectasis studied by the authors, 85 per cent were multiple segmental, and 30 per cent were bilateral. In this series, the lower division of the left upper lobe (lingula) was involved in about 60 per cent of those patients whose principal disease was in the left basal segments. On the right side the middle lobe was found to be involved with the right basal segments in 45 per cent of their cases. A frequent bilateral pattern to be found shows involvement of the right middle, the lower divisions of the left upper (lingula), and both right and left basal segments.

Clinical observations have shown that the severity of symptoms is closely related to the amount of tissue damaged. Experience also has demonstrated that good end-results parallel the surgeon's ability to eradicate all portions of lung that are diseased. If entire lobes are considered as surgical units, serious respiratory embarrassment will result if the disease is completely removed in bilateral cases; for example, the removal of the right middle lobe, both lower lobes, and lower divisions of the left upper lobe, leaves the patient with one complete and one partial lobe which may not be sufficient for anything more than an invalid existence.

The lack of standardization of bronchial nomenclature has led to much confusion. Jackson and Huber have proposed a nomenclature now widely accepted and used by the authors. The diagram on the opposite page illustrates this nomenclature.

Boyden has pointed out that, from a practical standpoint, most of these lung segments can be considered to be surgical units, but not strictly bronchovascular units. He found some arteries, mainly in the upper lobes, to be intersegmental and the veins to drain blood from adjacent segments.

Not infrequently the presence of a rudimentary fissure, or crevice, will indicate the topographical boundary of a bronchopulmonary segment. Surface markings suggesting rudimentary fissures become more evident after the lung has been collapsed. The involved segments may be contracted or already completely collapsed. There may be a difference in pigmentation. The diseased segment sometimes fails to deflate as rapidly as the normal segments and variations in intrapulmonic pressure by inflating and deflating the lung will also aid in identification.

Accurate delineation of the bronchopulmonary segments is accomplished by: (1) deflation of the lobe, (2) temporary occlusion of the bronchus, (3) reinflation of the lobe by means of increased positive intratracheal pressure.

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NOMENCLATURE FOR THE BRONCHI AND LUNGS

Adapted from CHEVALIER L. JACKSON and JOHN FRANKLIN HUBER Temple University School of Medicine



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R. MEDIASTINAL

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R.





L. LATERAL



L. MEDIASTINAL



Each bronchial branch is designated by the name of the subdivision of the lung supplied by it. L. DIAPHRAGMATIC SURFACE

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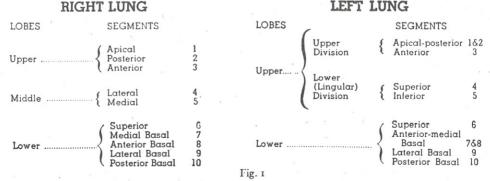
R. DIAPHRAGMATIC SURFACE

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A New Technique for Pulmonary Segmental Resection -Richard H. Overholt.

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A thorough knowledge of the intrahilar and related segmental anatomy of the lung is indispensable if one is to apply the surgical principles of individual treatment of anatomical structures in partial lobectomy. The anatomical pattern may vary and an anomalous distribution of bronchovascular structures may be found. These anomalies can be recognized and do not interfere with the treatment of the segment as a surgical unit.

During the past year the authors have developed a surgical technic which facilitates the removal of any bronchopulmonary segment. The use of clamps on lung tissue has been eliminated. Damage to healthy segments is avoided. The intersegmental plane is dissected so as to ensure removal of all diseased bronchi.

The segment is held within the lobe by four principle structures: the bronchus, the pulmonary artery, pulmonary vein, and <u>visceral pleura</u>. All of these structures can be identified and divided prior to the dissection of the intersegmental plane; then the development of this plane is made possible and simplified. The bronchi do not traverse this plane. For practical purposes, this plane is avascular. The supporting framework of connective tissue is loose, slightly elastic, and yields to gentle, blunt, and sharp dissection. Air leak of raw surface is negligible and self-sealing. Prompt healing of the denuded lung surface follows, as in other organs, since its blood supply has not been jeopardized or the tissue traumatized.

The technic as applied to any segment is briefly as follows:

1. Identify and divide the segmental pulmonary artery. In all segments except the apical posterior (left) and the apical and anterior (right), the major fisfure should be developed in such a manner as to find the segmental artery.

2. Identify and divide the segmental vein.

3. Identify and divide the segmental bronchus.

4. Determine the line of demarcation between segments by inflation and incision of visceral pleura completely around the lobe at this line.

5. Start development of intersegmental plane at the secondary hilum. Holding forceps are used to make traction on the bronchus, artery, and veins. Clamps on the lung tissue are not used and should be avoided because they may include ramifications of the bronchi. Dissection is done bluntly at first. Fibrous strands may be cut with scissors. Bronchi may be stripped between forefinger and thumb. The

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correct plane of cleavage is the one showing least resistance. From one to six intersegmental vessels may have to be ligated. Mosquito hemostats are used. If there is a question in the identification of a fine bronchus or a vessel, it is first cut and then, if it bleeds, ligated. If it happens to be a bronchus, the end is picked up again, and it is stripped out to its termination. Much of the dissection can be accomplished with the thumb and forefinger. It has been surprising to find that the structural attachment of the segment to the remaining portion of the lobe is so frail after the four supporting structures have been released. This completes segmental separation and treatment of the raw surfaces of the remaining segment. No attempt is made to fold over edges or use grafts.

6. Reamputation and meticulous closure of the segmental bronchus is then carried out. The authors, using stainless steel wire or silk, prefer to employ two interrupted mattress sutures and two or three end sutures applied over a free graft of parietal pleura.

After completion of the operation the pleural cavity is thoroughly washed out with saline warmed to body temperature. The thoracic cage is reconstructed by two chromic catgut No. 2 pericostal sutures placed subperiosteally. The intercostal nerves should be carefully avoided. Postoperative pain is greatly diminished by these precautions. Before the chest is closed a rubber catheter with lateral openings is placed in the pleural space and carried out through the lower end of the incision. Gentle suction is used for 24 to 48 hours. In the care of patients following segmental resection the same measures should be used that have been found to be of value after routine lobectomy. The two primary concerns are maintenance of airways and complete re-expansion of the remaining segments. Oxygen therapy is rarely needed.

From the 23 segmental resections that have been performed upon 21 patients for primary bronchiectasis, no deaths have occurred, and all of the patients have benefited greatly from the surgical intervention. All of the patients who had unilateral disease are free of symptoms. The age of the patients ranged from 7 to 56 years, with most of them in the second or third decades. The duration of the disease was from 4 months to 27 years. The amount of sputum varied from 1 ounce to 20 ounces daily. The outstanding clinical features in the order of severity were as follows: repeated colds, bouts of pneumonitis, hemoptysis, cough, and expectoration of purulent secretions. Foul sputum was present in 40 per cent of the cases.

In 4 cases bronchoscopy was necessary to aid in re-expansion. In each in stance watery secretions were found but no definite bronchial plug. Bronchoscopy

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also revealed submucosal edema of the orifice of the segment adjacent to the amputated one. The authors believe that this pathological finding explains the obstructive atelectasis in the absence of a bronchial plug. In times past, when all diseased segments were not removed, thick, tenacious sputum was a frequent postoperative finding. Following bronchoscopy, the condition of all of the patients improved and re-expansion was obtained. Empyema developed in 4 patients. One was treated locally with pleural aspiration and penicillin and cleared up entirely. The remaining three were drained. Bronchopleural fistula was demonstrated in two. In one of them a tension pneumothrorax which developed required an exploratory thoracotomy. This was performed 20 days after the segmental resection and revealed a pinpoint opening in the basal bronchial stump. This defect was repaired with interrupted sutures. Continuous suction was applied and re-expansion was obtained.

The incidence of complications in this series of segmental resections is greater than that which attended routine lobectomy, in which the incidence of empyema has been brought down to approximately 5 per cent. This series of pulmonary segment resections, however, is an original group and there is reason to believe that a reduction in complications will follow. It should be pointed out that at the present time the conservation of uninvolved pulmonary tissue far offsets any effects of a temporary pleural infection which may occur. Functional studies have not been done in this group of cases. In the future, when these studies can be undertaken, the authors are confident that comparative studies will reemphasize the importance of selective segmental resection for bronchiectasis. (Surg. Gynec. & Obst., Mar. 1947 - R.H. Overholt and L. Langer)

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<u>Histopathologic Study of the Anal Ducts</u>: Anal ducts lined with columnar epithelial cells are reported to exist in certain lower animals and in man. Their connection with the anal canal, their course through the internal anal sphincter, and their blind termination reaching at times as far as the iliac fossa have placed them "under suspicion" as avenues of the perianal spread of infection. This study was undertaken with a view to verifying or disproving certain statements relating to the incidence, position, and significance of these anal ducts.

The apparently normal anal canals of a number of human embryos and of one male stillborn infant were secured for study of the developmental aspects of the ducts. For comparative anatomic studies similar material was obtained from 10 monkeys. For the study of possible early inflammation in anal ducts of human adults, 100 specimens were selected from material from patients in whom removal of the rectum and anus had been performed because of sigmoidal or rectosigmoidal lesions. Finally the slides made during a previous study of

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100 cases of anal cryptitis in the human subject were reviewed to check on the presence of associated anal ducts and their possible role in the spread of anorectal inflammation. In each instance blocks were selected so as to include the mucosa of the rectum as well as of the anus.

This present study has amply confirmed the previous observations that epithelium-lined ducts are to be found in monkeys, human embryos, and human adults. Although few, they may be demonstrated rather easily in about 50 per cent of human anal canals. From openings in the anal crypts (most often posterior) they course outward and downward, often penetrating the internal anal sphincter. The majority are lined by transitional epithelium but definite mucus-producing cells maybe demonstrated in 10 per cent of them.

In order to understand the possible importance of the anal ducts as avenues for the spread of anorectal infection the fact of their existence must be realized. When these ducts appear in a "chance" section made from the anorectal region, being few and small, they may seem to be insignificant tubules having no apparent connection with the anal mucous membrane. Yet their peregrinations through the internal anal sphincter theoretically expose such remote locations as the ischiorectal fossae to the dangers of anal infection through their lumina or their periductal lymphatics. Therein lies their main interest, since this and other studies have not attributed to them any useful function in man. About 24 per cent of the ducts seen in this study show, focally or diffusely, a periductal inflammatory reaction. When ducts were found in material removed because of anal cryptitis, this incidence of periductal inflammation reached 89 per cent. The discovery of cases wherein the crypts were normal and the ducts inflamed perhaps signified a condition of residual infection which had previously existed also within the crypts. The authors believe that these ducts provide possible pathways for the lateral spread of such periductal infection once the latter is established, and it is concervable that ischiorectal abscess might have such a pathogenesis. Equally possible etiologically is the development of anal fistula, the area of predilection for which is the posterior portion of the anus which corresponds to the principal site found for the openings of the anal ducts. (Surg. Gynec. & Obst., Mar. '47 - G.L. Kratzer and M.B. Dockerty)

<u>Glaucoma Following the Ingestion of Sulfathiazole</u>: Penicillin has supplanted to a large degree the use of the sulfonamides in the therapy of many bacterial infections, but the use of sulfonamides is still so widespread that the report of an unusual reaction is deemed of interest.

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In 1943 Alvaro reviewed the effects other than anti-infectious of the sulfonamide compounds on the human eye. These included: (1) palpebral edema, (2) conjunctivitis, (3) chemosis, (4) scleral reaction, (5) iritis and numerous cells in the aqueous humor, (6) mydriasis, (7) cataract, (8) changes in the angioscotomas, (9) edema of the retina, (10) reduction of the visual fields, (11) retinal hemorrhages, (12) optic neuritis, (13) undefined or unidentified blurred vision, (14) transient ametropia, and (15) changes in accommodation and heterophorias.

A case report of acute congestive glaucoma in both eyes in a patient sensitive to sulfathiazole is reported and added to the list of ocular reactions to the sulfonamides.

A white woman, aged 24 years, was seen in the eye clinic of the station hospital, MacDill Field, Tampa, Florida, on the afternoon of 11 April 1945. She said that itching, light sensitivity, and burning of both eyes had been troublesome since she awakened that morning. Upon questioning, it was discovered that the patient thought she was sensitive to sulfathiazole, having developed red, burning eyes following the Ingestion of sulfathiazole prescribed for a sore throat in August, 1944. She had reported this suspected sensitivity to the drug to the medical officer who had seen her in her unit dispensary because of a sore throat on 10 April 1945, but he told her to try the drug again, and that if she proved sensitive it could be discontinued without harm.

Examination showed a mild conjunctivitis in both eyes with a few subconjunctival hemorrhages suggestive of a Koch-Weeks infection. Microscopic examination of a stained smear of the conjunctival secretions, however, revealed no organisms. Bacterial culture was reported negative after 48 hours. A mild astringent colyrium was prescribed, and the patient was sent back to duty. She was told to stop using the sulfathiazole and report back to the eye clinic in 48 hours.

By the next evening, the pain and redness of the eyes were worse and a severe headache had developed. She again reported to her dispensary. She was sent from the dispensary to the hospital for admission where the chief complaint was recorded as severe headache and pain in both eyes. General physical examination was negative except for the eyes. Temperature, pulse, and respiration were normal. Kahn test of the blood, urinalysis, and a complete blood count were normal.

She was seen in the eye clinic early on the morning of 13 April At this time, her eyes had the typical appearance of acute congestive glaucoma, and

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this diagnosis was made. There was edema of the eyelids, marked chemosis of the conjunctiva, mild iris edema, small irregular pupils that reacted sluggishly to light and accommodation, normal ocular fundi (as nearly as could be determined through the undilated pupils), and obviously increased intraocular pressure on palpation. Tension at 2:15 p.m. on 13 April was: right eye, 50 mm. and left eye, 60 mm. One drop of 1/4-per cent eserine salicylate was placed in each eye every 10 minutes until three doses had been given. At 3:30 p.m., tension of the right eye was 35 mm., and of the left, 22 mm. The considerable relief of the eye pain was accompanied by subsidence of the headache. However, the itching, burning, and general appearance of the eyes remained the same. One drop of 1/4-per cent eserine salicylate was placed in each eye every hour for 24 hours. On 14 April, the tension of the right eye was 38 mm., of the left eye, 35 mm. By 16 April, the chemosis had subsided; the pupils were of normal size and were reacting briskly to light and accommodation. Tension in both eyes was 28 mm. On 17 April, ocular tension was 24 mm. for the right eye and 20 mm. for the left eye. The small conjunctival hemorrhages were reduced in number.

Eserine was discontinued on 18 April. From that date until her discharge on 21 April, tension remained 22 mm. in each eye, and the eyes continued to improve until they were considered normal on the day of discharge.

The patient was seen again in the eye clinic two weeks and four weeks following discharge. The tension remained the same and the eyes appeared normal. It is felt that the manifestations of glaucoma in this case were unquestionably initiated by ocular sensitivity to the sulfathiazole, especially in view of the fact that the patient had suffered an ocular reaction from a previous use of sulfathiazole in August, 1944. (Am. J. Ophth., Feb. '47 - M.H. Fritz and M. Kesert)

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<u>Acute Porphyria</u>: This disease has not been widely publicized and hence its real incidence is not known. Two cases were reported in the Navy in 1945 and one case in 1946. In the latter case, in which death resulted, the diagnosis was suggested when it was noted that the patient's urine was of a dark mahogany color. Because of (1) the fact that cases may be missed since the disease can occur without discoloration of the urine, (2) the seriousness of the disease, (3) the vital importance of avoiding the use of barbiturates in this disease, and (4) the need for further information on the disease through the study and reporting of cases that may in the future be recognized in naval medical activities, the following material is presented from a recent review of the subject in the 11 January 1947 Lancet by Jørgen Jørgensen and Torben K. With of Copenhagen.

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Porphyria is divided into symptomatic, congenital, and acute forms. <u>Symptomatic porphyria</u> is the pathological excretion of porphyrins as a symptom of known diseases (infections, anemias, lead poisoning, etc.) and the only porphyrin excreted is coproporphyrin I. <u>Congenital porphyria</u> is a rare condition characterized by accumulation of uroporphyrin I in the blood and organs, especially the bones and skin, and excretion of this substance in the urine; small amounts of uroporphyrin III may also be present. This condition has no hereditary connection with acute porphyria. <u>Acute porphyria</u>, so-called, is the most important of the porphyrin diseases; it has been divided into toxic and idiopathic forms, but according to Waldenström this distinction is unnecessary. The disease manifests itself in acute attacks of abdominal pain, vomiting, and constipation, often accompanied by nervous symptoms and dark urine; but the underlying condition is a chronic disorder of pyrrole metabolism, which is latent between attacks. It is a disease of adults and seems to occur in all parts of the world.

The symptom suggesting the diagnosis of acute porphyria is usually the dark urine, and it is therefore important to know that the urine may be of entirely normal appearance in this disease. This is due to the fact that in acute porphyria the porphyrin is not excreted as such, but as a chromogen, named porphobilinogen, specific to acute porphyria, which is stable in alkaline urine but changed to a mixture of uroporphyrin III and the red pigment porphobilin in acid urine. Small amounts of uroporphyrin I may, however, occur. The abnormal substances are found only in the urine and - contrary to what happens in congenital porphyria - not in the blood or the organs. In fatal cases necropsy practically always shows nothing abnormal. Some cases of this chronic metabolic disorder never give rise to clinical symptoms and are known as latent porphyria; in such cases the excretion of porphobilinogen is most often permanent but may be intermittent. The investigations in Sweden have shown that acute porphyria is hereditary, probably of dominant mendelian type, and in investigations of the heredity it is important to recognize the latent cases.

It is well known that sulphonal and trional may give rise to attacks (toxic porphyria), and Waldenström is of the opinion that barbiturates also may provoke attacks in persons with latent porphyria. As attacks of acute porphyria are often fatal, it is important to avoid barbiturates in this condition, especially in manifest cases. Waldenström found a case-mortality of 2 cases out of 36 (about 5 and 1/2 per cent) when no barbiturates were given, as against about 50 per cent of the cases in most other published series, in which barbiturates were freely used.

Since the clinical picture of acute porphyria varies and may simulate other diseases, internists, surgeons, psychiatrists, and neurologists should watch for the disease and be able to diagnose it with certainty. This can be done only by urinalysis, which is quite simple. The urine of patients with acute, porphyria usually darkens on standing because its reaction is most often acid

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and the porphobilinogen is consequently transformed into uroporphyrin III and porphobilin. This process may take place in the bladder, for which reason the urine may be colored when freshly voided. If, however, the urine is made alkaline by giving the patients sodium bicarbonate, it remains the natural yellow color. Alkali therapy however does not reduce the excretion of porphobilinogen. If the darkness of the urine is due to some other cause, its color will not necessarily be changed by the administration of alkali.

In cases in which the urine is of normal color, the diagnosis has to be made by demonstrating porphobilinogen in the freshly voided urine. If porphobilinogen is not found, the patient cannot have an attack of acute porphyria. but he may have latent porphyria. Porphobilinogen is demonstrated by Ehrlich's benzaldehyde reaction; it gives the same reaction as urobilinogen with Ehrlich's reagent but is easily differentiated from this substance by the fact that it is insoluble in ether, whereas urobilinogen is readily extracted with ether in an acid medium. If the fresh urine gives the benzaldehyde reaction, about 2 ml. of 50 per cent acetic acid is added to about 20 ml. fresh urine in a separating funnel and extracted twice with about 40 ml. of ether. If the extracted urine still gives the benzaldehyde reaction, porphobilinogen is present. The diagnosis may be confirmed by demonstrating the porphyrin; but this is unnecessary because porphobilinogen is pathognomonic of acute porphyria. If the porphyrin concentration is sufficiently high, the urochlor reaction is positive. To 1 ml. of urine 2 ml. of concentrated hydrochloric acid is added; if the reaction is positive, a red color is seen, which, on addition of a drop of 3 per cent hydrogen peroxide - not too old a solution - in a few minutes gives way to yellow and later becomes grass-green and ultimately fades.

This reaction is common to all porphyrins and is positive also in symptomatic and congenital porphyrias.

If the urochlor reaction is negative, the porphyrin may be demonstrated after chromatography of the urine on anhydrous aluminum oxide. If closer chemical analysis is aimed at, more complicated procedures are required.

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Abstracts of Reports on Research Projects:

X-754 Rep. No. 1 3 Feb '47

Evaluation of SN 14,622 and SN 14,625 as Possible Antistreptococcal Agents,

In view of the importance of streptococcal infections in the Navy a study was decided upon to determine whether two analogues of pantothenic acid, SN 14,622 (d-Pantoyltauryl-pchloroanalide) and SN 14,625 (d-Pantoyltauryl-3,5-dibromoanalide) possess bacteriostatic and/or bactericidal activity against

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X-754 (Cont.) (Not Restricted)

streptococci with particular attention directed toward sulfonamide-resistant strains. The results of studies by other workers on the antistreptococcal activity of analogues of pantothenic acid indicated that valuable results might be expected from this investigation. Consideration was to be given also to the possible prophylactic or therapeutic value of these compounds in streptococcal infections in experimental animals.

The <u>in vitro</u> tests of Group A hemolytic streptococci with compounds SN 14,622 and SN 14,625 resulted in bacteriostasis of varying degrees with different strains of the group. Of 18 strains of different types and degrees of sulfonamide-resistant streptococci used in this study all were inhibited during 48 hours incubation with drug concentrations of from 0.01 mg. to 0.04 mg. per ml. of beef infusion broth, with the exception of three strains in SN 14,622 and one strain in SN 14,625. The sulfonamide-resistant strains as a group were as susceptible to these compounds as the nonresistant strains. This fact is of interest in view of the known inhibitory action of penicillin on many sulfonamide-resistant streptococci, and suggests the desirability of further studies.

Because the prophylactic or therapeutic efficacy of SN 14,622 and SN 14,625 in animals or human beings appears to be affected by the availability of pantothenate and because of incomplete knowledge of the variations that exist in the amount of pantothenate available in artificial media and in animals and human beings, considerable additional experimentation will be required to estimate any possible value of these two drugs in controlling human streptococcal infections. (Nav. Med. Res. Inst., Bethesda, Md - C. O. Edge and L. A. Barnes)

(Not Restricted)

X-756 Rep. No. 3 6 Feb '47 <u>Improved Subsurface Water-Sampling Apparatus</u>: In connection with investigations of the causes and means of control of diarrheal diseases and dysenteries ashore and afloat, it was believed desirable to obtain samples of harbor water at various depths. Preliminary inquiries and visits to certain water treatment and sewage disposal plants failed to elicit information concerning the availability of a sampling device suitable to the needs of the project; it was felt that the apparatus used in the Winkler process would be too cumbersome and that other devices would not be adequate for the anticipated purposes.

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X-756 (Cont.) Therefore a simple, lightweight, and inexpensive subsurface water-sampling apparatus was developed. It consists of a brass housing, to hold the sample bottle, attached to a brass pipe through which passes a rod for removing and replacing the stopper. The length of the pipe and rod can be regulated as desired by the number of sections of each used.

The apparatus was given a test in a diving tank when the water was at rest and when it was agitated by running compressed air near the sampler. It was found that a period of five seconds with the sample bottle open permitted an adequate amount of water to enter. Additional trials using depths of six, nine, twelve, and fifteen feet were made from a small boat on a river at locations selected to test the operation of the device at different rates of current flow; all tests were satisfactory. (Nav. Med. Res. Inst., Bethesda, Md. - L. A. Barnes and J. F. Bronson)

<u>NOTE:</u> Those interested in seeing copies of the complete reports should address their request to the Research Division, BuMed.

Opinions or conclusions contained in these reports are those of the authors. They are not to be construed as necessarily reflecting the views or the endorsement of the Navy Department. Reference may be made to those reports marked "Not Restricted" in the same way as to published articles noting authors, title, source, date, project number, and report number. No part of the content of RESTRICTED reports may be published, reproduced, or referred to in articles for publication without permission obtained through the Bureau of Medicine and Surgery.

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<u>Policy Regarding Assignment of Personnel to Duties Dealing Primarily</u> <u>with the Materiel Aspects of Medical Department Logistics</u>: 1. The recent hostilities emphasized the military axiom that, to wage war successfully with the minimal loss of human life, it is imperative that the necessary forces, facilities, services and materiel be at the places where they are needed, when they are needed and in the numbers or quantities required. The term "logistics" encompasses the methods by which this required varied support is determined and provided, and the means by which its accomplishment is executed. The realization of this dictum requires the coordinated application of many specific knowledges, skills and technics throughout the strata of an integrated logistics organization.

2. The availability of materiel largely determines the effectiveness of performance of all other logistics support functions, in peace or in war; thus the scope and timing of military operations is dependent upon the materiel means which will be available. Adequate logistic accomplishments, which include the availability and timely supply of the materiel required, can only be attained when there is realistic correlation of the strategic-tactical concepts, the materiel and manpower capabilities, and the nation's productive capacities.

3. The primary functions of the Medical Department of the Navy in peace and in war are, in the broad sense, all logistic in nature--designed to provide the required medical support for the naval forces ashore and afloat. For the effective discharge of these paramount responsibilities of the Bureau of Medicine and Surgery--the proper care of the sick, the injured or wounded, the prevention of disease, and the maintenance of the highest attainable degree of physical fitness--it is mandatory that there be efficient accomplishment of all aspects of its logistic performance. Here, again, the materiel aspect of logistics effort is of utmost and determining importance. It is therefore imperative that a cadre of specially trained and experienced medical and dental officers in the ranks of Lieutenant-Commander and above be available at all times to furnish effective planning, direction and control in the realm of medical department materiel logistics system in peacetime, and will constitute the essential source of the key personnel for expansion of the system during war.

4. In order that medical and dental officers may assume the above responsibility and receive due recognition for this important assignment, and yet maintain or improve their professional proficiency, the following policies regarding duty in the medical department logistics system is announced herewith:

(a) After satisfactory completion of a tour of duty in the medical department materiel logistics system, medical officers will be assigned to duty in Naval Hospitals, or to postgraduate instruction courses in Naval Hospitals or civilian medical

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institutions; similarly, dental officers will be assigned to dental clinics or to postgraduate instruction.

- (b) Medical and dental officers with seniority normally calling for administrative assignment may request consecutive logistic system billets.
- (c) Senior and Junior standards will be established for certification as qualified medical logistic specialists. An appropriate symbol will appear opposite the officer's name in the Register of Commissioned Officers as is done for other recognized specialties.
- (d) Elementary logistics courses will be included in the curriculum of the Naval Medical School and the Naval Dental Schools.
- (e) Junior certification will be awarded to officers who have satisfactorily completed a tour of duty in the echelons of the medical logistics system, have done the necessary collateral reading and have submitted an acceptable thesis upon an assigned subject.
- (f) Senior certification will be awarded to graduates of the Industrial College of the Armed Forces, the Naval War College Logistics Course, or the Armed Forces Staff College, or to officers with equivalent service experience.

5. The following assignments are designated as billets in medical department materiel logistics, and will be filled by qualified officers of appropriate rank:

			Medi Offic		Denta <u>Office</u>	
(1) Bureau of Medicine and Surgery					
	# Chief of Materiel Division		1#	:		• =
	Assistant Chief Materiel					
	Division and Requirements Officer		1			
- I.	Dental Materiel Officer				1	
	Materiel Projects Officer	· · · · · · · · ·	1			
	Professional Supervisors for			5		
	Materiel		3	1990 A.	1	
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Bumed News Letter, Vol. 9, No. 7 RESTRICTED (Not Restricted) Medical Dental Officers Officers (2) Assistant Secretary of Navy, Materiel Division Medical Materiel Officer 1 (3) Army-Navy Medical Procurement Agency # Director or Deputy-Director (1)# Army-Navy Medical Procurement Office Commanding Officer or Executive Officer 1 Division or Branch Heads 2 1 (4) Continental Shore Establishment Naval Medical Supply Depots, Brooklyn, N.Y., and Oakland, California: Medical Officer in Command 2 2 Executive Officer 2 Dental Materiel Officer **Requisitions and Requirements** Review (5) Extra-Continental Shore Establishments Naval Medical Supply Depots, Pearl Harbor, T. H., and Guam, M. I. 2 Medical Officer in Command Executive Officer and Requisitions 2 and Requirements Review Officer Dental Advisor (6) Fleets Commander in Chief Fleets. Atlantic and Pacific: Logistics Staff** Commander Service Forces. Atlantic and Pacific: 2 Force Medical Officer** 2 2 Logistic Assistants** (7) U. S. Marine Corps Commanding General, FMF, Atlantic and Pacific: Logistics Staff**

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		(N Medical <u>Officers</u>	ot Restricted) Dental <u>Officers</u>
	Commanding General Supply Service, FMF, Atlantic and Pacific: Force Medical Officer** Logistic Staff**	2*	*
(8)	Industrial College of the Armed Forces Student Officers	2	1
(9)	<u>Naval War College Logistics Course**:</u> Staff (Instructor)** Student Officers**	$\frac{1}{2}$,	1
(10)	Armed Forces Staff College**: Staff (Instructor)** Student Officers**	1 2	

Same officer fills both billets

* Assignment regulated by requirements of service

**Covers the broad field of logistics of which materiel logistics is a part.

6. Medical and dental officers in the ranks of Lieutenant-Commander or above who desire assignment to duty in the medical materiel logistics system are requested to submit applications through channels to the Bureau of Medicine and Surgery, Navy Department, Washington 25, D.C.

--BuMed. C. A. Swanson

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<u>Radiological Safety Courses and Need for Medical Officers for Advanced</u> <u>Training:</u> Because the medical aspect of radiological safety is becoming increasingly important, the Bureau of Medicine and Surgery is planning to issue a pamphlet covering a basic course of indoctrination that will be made available in the near future to all personnel of the Medical Department (including Reserve). However, it will be necessary for a limited number of officers to have a much more extensive knowledge of the subject than can be included in the basic course. Applications from medical officers of all ranks to participate in an advanced course in <u>Radiological Safety</u> are requested by the Bureau of Medicine and Surgey.

(Professional Div., BuMed)

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<u>Reserve Medical Officers Needed for Combat Air Group Training Course</u>: Reserve medical officers will be needed for a two weeks' training course of Naval and Marine combat air groups of the Naval and Marine Air Reserve Training Commands. It is anticipated that the first of these periods will occur in the month of June, 1947. Interested officers below the rank of captain are invited to communicate with the Staff Medical Officer of CNAResTra, NAS, Glenview, Ill., stating geographic area where duty is desired, and the date which will be most convenient to attend. (Personnel Div., BuMed)

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<u>Opportunities for Naval Reserve Medical Officers</u>: The attention of Reserve medical officers is invited to the opportunity to return to <u>active duty</u> at one of the major naval air stations of the Naval Air Reserve Training Command or at one of the Naval Air Reserve Training Units (NARTUS) listed below:

NAS, Atlanta, Ga. NAS, Columbus, Ohio NAS, Dallas, Texas NAS, Denver, Colo. NAS, Glenview, Ill. NAS, Grosse Ile, Mich. NAS, Los Alamitos, Calif. NAS, Memphis, Tenn. NAS, Miami, Fla. NAS, Minneapolis, Minn. NAS, New Orleans, La. NAS, New York, N.Y. NAS, Oakland, Calif. NAS, Olathe, Kas. NAS, Squantum, Mass. NAS, St. Louis, Mo. NAS, Willow Grove, Pa. NARTU, NAS, Anacostia, D.C. NARTU, NAS, Jacksonville, Fla. NARTU, NAS, Norfolk, Va. NARTU, NAS, Seattle, Wash.

Reserve medical officers who are interested in <u>active duty</u> at one of the stations or units listed above should initiate letters to the Bureau of Naval Personnel, via Chief of Naval Reserve Air Training, Naval Air Station, Glenview, Ill., and BuMed, listing three or four stations at which duty is desired in order of preference. Personnel are desired in rank of commander and below in the Medical Corps. However, captains may apply for this duty and, in their applications, request a waiver of the rank requirement.

Officers qualifying for the above billets may terminate the tour of duty at their own request. It is anticipated that all orders to flight surgeons will include duty involving flying. Government quarters are available at several of the major naval air stations.

Naval Reserve flight surgeons who desire to join one of the Naval or Marine combat air groups of the Organized Reserve training at one of the

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stations listed above should contact the local commanding officer for additional information. Two months pay per year is granted for attendance at all training periods. (Personnel Div., BuMed)

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<u>Changes to be Made in Copies of Manual of the Medical Department</u>: Certain changes in the Manual of the Medical Department have been directed as specified in Circular Letter 47-32, page 34.

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Public Health Foreign Reports:

Disease	Location	<u>Date</u> management	No. of Cases
Cholera	Indochina (French) Cambodia	January '47	230 (147 fatal)
Plague	Madagascar	Dec. 11-31, '46	63 (61 fatal)
Smallpox	Indochina (French)	January '47	373 (152 fatal)
Typhus Fever	Bulgaria Eritrea Rumania	Jan. 15-21, '47 Jan. 26-Feb. 1, '47 Jan. 8-15, '47 Jan. 19-25, '47	43 (6 fatal) 30 (5 fatal) 369 400

(Pub. Health Reps., March 7 and 14, '47)

D, 16, 18, 17), the Folloman

To: All Ships and Stations 21 February 1947 (Not Restricted) Subj: School of Dental Practitioners, Guam, Marianas Islands, establishment of.

1. The following activity is established effective 28 January 1947:

* *

School of Dental Practitioners, U.S. Naval Medical Center, Guam, Marianas Islands.

7302-300

2. This activity, under an officer in charge, is a subordinate unit of the U.S. Naval Medical Center, Guam, and under the management control of the Bureau of Medicine and Surgery.

3. Bureaus and offices concerned take necessary action. --SecNav.

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Circular Letter 47-29 12 March 1947

(Not Restricted)

To: All Medical and Dental Officers

Subj: <u>Policy Regarding Assignment of Personnel to Duties Dealing Primarily</u> with the Materiel Aspects of Medical Department Logistics:

This letter from the Chief of BuMed, because of its content, is placed with the Notice Section. See page 26.

Circular Letter 47-30 12 March 1947 (Not Restricted)

To: Medical Officer in Command, All Naval Hospitals.

Subj: <u>Special Report of Funds and Personnel for Fiscal Year 1947 for</u> <u>Budgetary Purposes</u>:

Encl: 1. (HW) Sample form for reporting obligations. 2. (HW) Sample form for reporting personnel.

This letter from the Deputy and Assistant Chief of BuMed requests that addressees furnish to BuMed certain information that will be of assistance to the Bureau in the preparation of its 1949 estimates for early submission to budget groups.

Circular Letter 47-31

13 March 1947

(Not Restricted)

- To: Commandants, All Naval Districts (less 10, 15, 16, 17), the Potomac River Naval Command, and the Chief of Naval Air Reserve Training.
- Att: District Medical and Dental Officers and all Medical Department Personnel concerned.
- Subj: <u>Training Program (in Armories) for Naval Reserve Hospital Corps</u>-<u>men</u>:
- Encl: (A) (HW) Ten (10) copies "Outlines for Naval Reserve Curricula, Hospital Corps, Class "P", "A", and "B".

1. Advance copies of Enclosure (A) are forwarded herewith for the information and guidance of all Medical Department personnel concerned with the implementation of the Training Program for Naval Reserve Hospital

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(Not Restricted) Corpsmen. Further copies as required will be furnished upon request.

2. Enclosure (A) lists and outlines the curricula for armory instruction of enlisted members of the Hospital Corps attached to the various components of the Naval Reserve. These curricula are being prepared for printing and will be mailed to addressees when completed.

3. The training program for enlisted personnel of the Hospital Corps is patterned after that of the Regular Navy. As soon as a new man is enlisted he will be assigned to a Recruit Class (for a period of indoctrination, drawing clothing, etc. - no formal curriculum provided), then to the Class "P" school for the initial instruction established for Hospital Apprentices. The Class "P" curriculum consists of 96-45 minute periods, which, at the rate of two periods per night, will require about one year. Upon satisfactory completion of this course the man will be ready for advancement to Hospital Apprentice First Class, and assignment to the Class "A" School.

4. The Class "A" curriculum provides for 160-45 minute periods, and will require about 1 year, 8 months. Satisfactory completion of this course will cover the armory training requirements for advancement to Pharmacist's Mate Third or Second Class and assignment to the Class "B" school. Grades attained in subject matter and authorized complements will be factors in determining whether a man earns Third or Second Class Pharmacist's Mate United States Naval Reserve.

5. The Class "B" curriculum provides for 240-45 minute periods, requiring about two and one-half years. Satisfactory completion of this course, grades attained in subject matter, and authorized complements will be factors in determining whether a man is advanced to Pharmacist's Mate First Class or to Chief Pharmacist's Mate, United States Naval Reserve.

6. Specific requirements for advancement, including time in rating, as established in Part H, Bureau of Naval Personnel Manual, and current directives will govern advancements in rating of enlisted personnel of the Hospital Corps, Naval Reserve.

7. In view of the manner in which the various curricula are sectionalized, it will be practical for a new man to enter any course at almost any time regardless of when the course actually commenced. If any man is able to demonstrate by examination that previous experience or training has qualified him in one or more of the sections, his Division Instructor may, in his discretion, exempt him from taking part of the course. The essential purpose of this training program is to maintain the training level of Hospital Corpsmen in the Naval Reserve as far as possible on a par with that of the Regular Navy.

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(Not Restricted)

8. The courses of instruction outlined in Enclosures (A) are intended for use in the instruction of enlisted Hospital Corpsmen in both Organized Units and Volunteer groups of the Naval Reserve.

9. The authorization of an annual two-weeks training cruise for enlisted Hospital Corps personnel of the Volunteer Naval Reserve at major Medical Department activities is under consideration.

10. Allowance lists of authorized Medical Department supplies and equipment for armory instructional purposes based on the curricula outlined in Enclosures (A) are being prepared by the Bureau and will be forwarded to District Commandants for implementation in the near future.

--BuMed. C.A. Swanson

Note: Because of size, a copy of enclosure to addressees is not reprinted in Bumed News Letter.

Circular Letter 47-32 13 March 1947

(Not Restricted)

ComThree, Four, Nine, Twelve and Thirteen. To:

Report of Naval Reserve Dental Program, establishment of. (Change Subj: in MMD No. 2).

1. In order for the Bureau to have information available to administer an effective Dental Reserve Program, each district having a Reserve Dental Liaison Officer shall submit a monthly letter report in accordance with the following paragraphs which shall be added to the Manual of the Medical Department:

(Not Restricted)

Add the following paragraph:

51454

Monthly Report of Naval Reserve Dental Program .----5145A.1. Each Naval District having a Naval Reserve Dental Liaison Officer shall submit, in duplicate, at the close of each month, a Monthly Report of Naval Reserve Dental Program.

5145A.2. The first report submitted by a District shall summarize the progress made in the dental reserve program up to that time, and shall include a list of activated or authorized Volunteer and Organized units and the names of the dental officers attached. Subsequent reports shall contain any additional units authorized or activated and the names of additional reserve dental officers assigned and any other data which may be of value to the Bureau in administering the program.

Add the Monthly Report of Naval Reserve Dental Program to the table "Tabulation of Reports," page 479, MMD.

--BuMed. C.A. Swanson

Circular Letter 47-33 . 17 March 1947

(Not Restricted)

To: All Ships and Stations.

Subj: BuMed Material Requisition, NavMed-4 (Rev. 12-46); preparation and submission of.

Ref: (a) BuMed Cir Ltr 46-68, 15 Apr 1946.

- (b) BuMed Cir Ltr 46-156, 28 Oct 1946.
- (c) Articles 1164 and 1166, Navy Regulations.
- (d) BuMed Cir Ltr 44-18, 28 Jan 1944.

This letter from the Chief of BuMed, a copy of which is to appear in the 31 March 1947 Navy Department Bulletin, gives complete instructions for the preparation and submission of the revised NavMed-4 (12-46). The new forms are available at the nearest District Publications and Printing Office and upon receipt all previously printed forms are to be destroyed. This letter cancels references (a) and (b).

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Circular Letter 47-34

20 March 1947

(Not Restricted)

To: Naval Hospitals.

Subj: Facilities of Red Cross Activities, Maintenance of.

Ref: (a) OpNav ltr OP30-ad Serial 596330, dated May 29, 1943. (b) Article 1478 Nav Regs 1920-

1. Information received in this Bureau indicates the existence of a misunderstanding pertaining to the status of American National Red Cross activities at Naval Hospitals.

2. Commanding Officers are authorized by reference (a) and (b) to provide suitable space for activities of the Red Cross attached to the Command.

3. The maintenance, including cleaning supplies and services, of spaces so assigned within the command, will be provided by the hospital at no charge to the Red Cross.

> --Deputy and Assistant Chief of Bureau H.L. Pugh

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